

[4-01: Support for Water and Human Health Studies] *Edit as appropriate*
ADDITIONS TO WORK ASSIGNMENT STATEMENT OF WORK

Additional Task Descriptions[TC \12 "]

Task 1. The following line shall be added as needed to existing statement of work: The Contractor shall include estimates of the dollars and hours expended for Task [#] in their Monthly Report.

Task [#]. Literature review on epidemiological studies of health impacts associated with paraquat exposure

1. The contractor shall conduct a literature search and assemble a database of references (including abstracts) in an EndNote Library of epidemiological studies examining the human health effects associated with paraquat exposure.

The contractor shall conduct a literature search of the peer-reviewed, published literature in PubMed, Web of Science, and ScienceDirect for epidemiological studies that have examined and measured human health effects associated with paraquat exposure as defined below. The contractor shall document search terms, databases used, search returns, and dates of arch. Examples of search terms shall include, for example: paraquat, paraquat synonyms, environmental exposure, occupational exposure, in combination with health-related terms such as “health” or “health effects” and types of epidemiological studies such as case control, cohort, cross-sectional. Prior to conducting said literature search with the contractor-developed search terms, the contractor shall consult with EPA for advice and suggestions on the search terms and databases used.

In addition to database searches, reference lists of selected relevant papers will be reviewed for additional relevant papers. Once key authors are identified, searches shall be conducted and additional publications by these authors reviewed for relevance. Citations provided in these papers will also be searched for additional relevant studies.

For the EndNote Library, papers shall be included that meet the following criteria:

- Population of interest: The population studied must be humans with no restrictions, including no restrictions on age, lifestage, sex, country of residence/origin, race/ethnicity, lifestyle, or occupation
- Exposure: The exposure studied must be to paraquat in any application via any route of exposure
- Comparator: Exposed or case populations must be compared to a population with low/no exposure or to non-cases to arrive at a risk/effect size estimate of a health outcome associated with paraquat exposure

- Outcome: All reported human health effects, with no restrictions on human system affected. These effects could be based on survey or other self-report, medical records, biomarkers, publicly available health data, or measurements from human sample populations.

Potential studies may include, for example, occupational studies, community studies, and large cohort studies. Study designs may include any epidemiological study design (for example, ecological, cross-sectional, case-control, cohort, and intervention study).

For the purposes of this review, papers which focus exclusively on environmental or ecological effects -- with no measurement of potential human health effects -- will not be included. Risk assessments (which do not directly measure a health effect) shall not be included. Other exclusion criteria include: articles not available in full text; articles not peer reviewed; studies on non-human subjects; in-vitro studies; fate and transport studies; experimental model system studies.

Examples of appropriate papers include:

Hoppin, J. A., Umbach, D. M., London, S. J., Alavanja, M. C., & Sandler, D. P. (2002). Chemical predictors of wheeze among farmer pesticide applicators in the Agricultural Health Study. *American Journal of Respiratory and Critical care medicine*, 165(5), 683-689.

Dalvie, M. A., White, N., Raine, R., Myers, J. E., London, L., Thompson, M., & Christiani, D. C. (1999). Long-term respiratory health effects of the herbicide, paraquat, among workers in the Western Cape. *Occupational and environmental medicine*, 56(6), 391-396.

Kamel, F., Tanner, C. M., Umbach, D. M., Hoppin, J. A., Alavanja, M. C. R., Blair, A., ... & Ross, G. W. (2007). Pesticide exposure and self-reported Parkinson's disease in the agricultural health study. *American Journal of Epidemiology*, 165(4), 364-374.

2. The contractor shall obtain electronic .pdf copies of selected references after approval by EPA.

After providing the EndNote Library, the EPA will review the database and provide guidance to obtain specific references for further review.

3. The contractor shall prepare a written report (MS Word document) reviewing, summarizing, and assessing the quality of the assembled literature. Key elements shall also be summarized in tabular form (Excel document or equivalent). The review shall contain the following elements:
 - Details of literature search
 - Search terms, databases searched, number of articles returned, date of literature search, and selection criteria as well as qualifications of those conducting the search

- A detailed summary and evaluation of each paper included in the review. The evaluation shall address the following areas:
 - Summary
 - Study overview: study design, study dates (including but not limited to date exposure ascertained, date follow-up ended, study results and conclusions, and if this is an update to a previously published study)
 - Study details: exposure measurement (including but not limited to: self-administered questionnaire, dust sample collection, personal sampling device), outcome ascertainment (including but not limited to: self-report, doctor's confirmed self-report, state cancer registry), number of participants (n), number exposed and/or number of cases, number in reference (un-exposed and/or control) group, effect measure (including but not limited to: odds ratio (OR), relative risk (RR), hazard ratio (HR), incident rate ratio (IRR), standardized mortality ratio (SMR) and associated estimate of uncertainty and/or statistical significance (including but not limited to: confidence interval (CI), p-value), confounders considered, and methods of analysis (including but not limited to: Poisson regression, logistic regression, multiple linear regression).
 - Strengths and limitations discussed in the paper including author-identified biases
 - Evaluation
 - Identify and discuss strengths and weaknesses in the study design
 - Identify and discuss strengths and weaknesses in the statistical analysis and other data-related issues (e.g., binning of data, classification approaches, etc.)
 - Identify and discuss biases (including study design issues related to recall and other epidemiological biases from uncontrolled confounding and other biases) which may have affected the result and may not be reported by the authors
 - Reference citations from other epidemiology studies that conflict with the reported results/conclusions
 - Discussion of alternative reasons for the observed results including both those raised by the author(s), if any, as well as a discussion of potential alternative explanations neglected or not mentioned by the author(s)
 - An overview (provide citation) of other commentary, letters or follow up papers published in response to the paper

Additional Deliverables

Task [#]. Deliverable [#]. The Contractor shall deliver an EndNote Library with the results of the literature search, described above, within 30 calendar days of the receipt of this Task, unless otherwise mutually agreed upon. After providing the EndNote Library, the EPA will review at the database and provide guidance to obtain specific references for further review. The Contractor shall provide all of the papers selected for further review in .pdf format.

Deliverable [#]. [SEQ CHAPTER \h \r 1]The Contractor shall prepare a report reviewing, summarizing and assessing the quality of the assembled literature using the elements listed above. A draft report is due 90 calendar days after the EPA has provided guidance on which references merit further review, unless an alternate date is otherwise mutually agreed upon. Approximately midway through this time period, the contractor and EPA will meet (either in person, via teleconference, or via webinar) at a mutually agreeable time to discuss progress and to provide an update on the status and any issues or concerns that might exist. The EPA will provide comments on the draft report within 21 calendar days after receipt. A final report, incorporating any EPA comments, is due within 15 calendar days of receipt of the EPA's comments. The Contractor shall deliver the report and all supporting documentation in a format that has been approved by the WACOR.